

### **REMARKS**

Claims 1, 3-5, and 7-23 are pending.

#### **The rejection under 35 U.S.C. §103(a)**

Claims 1, 3-5, and 7-23 were rejected as being obvious over Webb et al., 1997, The Lancet 349:1137-1141 (Webb) in view of Waters et al., 2000, J. Clin. Oncol. 18:1812-1823 (Waters) and U.S. Patent No. 6,214,986 (Bennett).

The Applicants continue to believe that the claims are not obvious. None of Webb, Waters, or Bennett, alone or in combination, suggests a cycle of therapy as short as 3 to 9 days, as recited in the present claims. As explained in the Novick Declaration, filed April 30, 2007, neither Webb nor Waters teaches or suggests changing the treatment regimen to anything shorter than a two-week course of therapy. See paragraphs 8-23 of the Novick Declaration

Bennett does not cure this deficiency of Webb and Waters. Bennett is not directed to the administration of bcl-2 oligonucleotides and thus would be viewed by one of ordinary skill in the art as being less pertinent than the disclosures of Webb and Waters. Furthermore, Bennett's teachings with respect to duration of therapy are so broad as to be essentially meaningless. See the Office Action, page 7 (discussing Bennett): "with the course of treatment lasting from several days to several months ... may be given once or more daily, weekly, monthly or yearly, or even once every 2 to 20 years." It is not possible to derive a suggestion that the two-week cycle of therapy disclosed in Webb should be shortened to 3 to 9 days from a disclosure of treatment that ranges from daily to every 20 years.

The Office Action, at pages 5-6, relies on the concept of inherency to conclude that Patient 6 of Webb was treated for cancer. See page 5, 1<sup>st</sup> paragraph: “[I]t is the Examiner’s position that at day 7, the cancer in Patient 6 was inherently treated ...” See also the sentence bridging pages 5 and 6: “[T]he PTO can require an Applicant to prove that the prior art products do not necessarily or inherently possess the characteristics of his [her] claimed product.”

Continuing with this inherency argument, the Office Action cited M.P.E.P. §2112.01, *In re Best*, 562 F. 2d 1252, 195 U.S.P.Q. 430 (CCPA 1977) and *In re Spada*, 911 F. 2d 705, 15 U.S.P.Q. 2d 1655 (Fed. Cir. 1990) as standing for the proposition that “[I]t falls to Applicant to determine and provide evidence that the administration of a bcl-2 antisense oligonucleotide to Patient 6 for 7 days disclosed by Webb et al. would or would not treat cancer as instantly claimed.” (Office Action, page 6).

The Applicant respectfully submits that the Office Action is misapplying the law. M.P.E.P. §2112.01, *Best*, and *Spada* are all directed to product claims and whether a prior art disclosure inherently anticipates such product claims. The present claims are method claims and what is at issue in this rejection is not anticipation, but obviousness.

The Office Action is using the supposedly inherent treatment of cancer in Patient 6 as motivation to shorten treatment cycles and arrive at the presently claimed limitation of cycles of 3 to 9 days. This is an improper use of the concept of inherency. An inherent characteristic may not be used as motivation to make changes in the prior art. This is because such an inherent characteristic is not necessarily known and obviousness cannot be predicated on an unknown characteristic.

See, e.g., *In re Spormann*, 363 F.2d 444, (CCPA 1966). In *Spormann*, the claims at issue were directed to a process of producing sulfite with low levels of sulfate. The claims were rejected over a combination of references generally pertaining to the production of sulfite where one reference disclosed a process which the Board of Patent Appeals argued inherently would have produced low levels of sulfate. The Court of Customs and Patent Appeals reversed the Board, holding that it was improper to use the inherent characteristic of low sulfate levels as motivation to arrive at the claimed invention.

The board apparently thought that the minimizing of sulfate production would be inherent in the process of Friedrich et al. However, this is not support for a rejection for various reasons. Friedrich et al. make no mention of it, as the board conceded. ... As we pointed out in *In re Adams*, 356 F.2d 998, 53 CCPA, the inherency of an advantage and its obviousness are entirely different questions. That which may be inherent is not necessarily known. Obviousness cannot be predicated on what is unknown.

363 F.2d at 448.

As pointed out by *Spormann*, an unknown property cannot motivate one to make an invention that depends on the unknown property. Nor can one have a reasonable expectation of success when success depends on an unknown property.

The Office Action appears to be requiring the Applicant to prove that the bcl-2 antisense oligonucleotide of Webb did not inherently possess the ability to treat cancer (“[I]t falls to Applicant to determine and provide evidence that the administration of a bcl-2 antisense oligonucleotide to Patient 6 for 7 days disclosed by Webb et al. would or would not treat cancer as instantly claimed.”; Office Action, page 6). In other words, the Office Action is requiring the Applicant to prove that the

product used in the claimed methods does not have the very property which makes the product useful in the claimed methods.

This cannot be correct. If the Office Action were correct, then it would be impossible to obtain claims to a new method of using an old product, since the old product would always inherently possess the ability to be used in the new method. Since it is clear that one can obtain claims to a new method of using an old product, the Office Action's position must be wrong.

In addition to being inappropriate to an obviousness rejection, the Office Action's inherency argument is untenable because there is no evidence to support the position that Patient 6's cancer was treated at day 7. Patient 6 received the full, two-week course of therapy. Therefore, any improvement in the condition of patient 6 can only be attributed to that full, two-week course of therapy. It is irrelevant for this obviousness inquiry that patient 6's bcl-2 levels may have been reduced after 7 days, since nothing ties those 7 days of treatment to any success in treating cancer. See paragraph 12 of the Novick Declaration: "One would not know whether the total infusion of 14 days was necessary to provide treatment of cancer or whether infusion of 7 days of therapy would be sufficient."

Assuming for the sake of argument that Patient 6 showed improvement, there is no evidence in Webb that, had patient 6's course of therapy been stopped after 7 days, patient 6 would have shown the same, or any, improvement. See the Office Action, page 5: "Webb et al. are silent regarding whether cancer was treated in Patient 6 after the 7-day course of bcl-2 antisense oligonucleotide treatment." This silence means that an assumption that Patient 6's cancer was inherently treated at day 7 lacks any evidentiary basis.

Despite such lack of evidentiary basis tying the reduction in bcl-2 levels at 7 days to any positive treatment outcome, the Office Action relies on a supposed connection between the reduction in bcl-2 levels at 7 days and eventual positive results to support this rejection. See page 13 of the Office Action:

It is the Examiner's position that, based on the results from Patient 6, one skilled in the art would have been motivated to shorten the generally accepted 14-day course of therapy to, for example, 7 days, since Webb et al. teach that at day 7, bcl-2 levels in the lymph nodes were reduced in Patient 6, compared with pretreatment. Because Patient 6 eventually exhibited evidence of tumor shrinkage and had a decrease in the number of circulating lymphoma cells, one skilled in the art would have been motivated to shorten the course of therapy to 7 days to determine whether this brief course of therapy was responsible for the favorable results seen in Patient 6. [underscoring added]

The Applicants respectfully submit that this supposed connection, since it is unsupported by evidence, cannot support an obviousness rejection.

The Applicants note that, even after two weeks of treatment, Webb states that Patient 6 “did not satisfy definition of partial response.” See the table at the bottom of the right column of page 1138 of Webb. Later, on page 1139, right column, Webb characterizes Patient 6's results as “near partial responses in right auxiliary and mediastinal lymph nodes, but in the larger lymph-node mass within the abdomen, response was negligible.” See also the Novick Declaration, at paragraph 12: “[P]atient 6 did not show a promising cancer response.” Thus, Patient 6's cancer cannot be said to have been treated, even after two weeks of treatment, and the Office Action mischaracterizes the results for Patient 6 when it states that those results were “favorable” in the above quote.

Despite its irrelevance to the question of obviousness, this reduction in bcl-2 levels forms the basis for the supposed motivation to make the claimed invention.

See the Office Action, page 8: “One of ordinary skill in the art would have been motivated to devise a method of treating cancer in a human comprising administering a bcl-2 antisense in a cycle of therapy consisting of 3 to 9 days since Webb et al. taught the reduction of bcl-2 protein levels in the lymph node aspirates of Patient 6 after the 7-day administration of a bcl-2 antisense oligonucleotide.”

Rather than supporting a case for obviousness, the results for Patient 6, and for the other patients in Webb, teach away from the present invention. These results, which were “not impressive” (see the Novick Declaration, paragraph 9), suggest, if anything, that cycles of therapy should be lengthened beyond the 14-day cycles of Webb instead of shortened to the 3 to 9 day claimed cycles. See the Novick Declaration, paragraph 14: “In my opinion, one skilled in the art reading Webb would not be motivated to shorten the course of therapy, but rather would be motivated to continue with a longer course of therapy ...” [underscoring in original]

The Applicants note that the Office Action states, at page 13, that one skilled in the art would be motivated to shorten the course of treatment because of Webb’s statement that “[O]ur findings are encouraging and warrant further investigations of bcl-2 antisense therapy in cancer treatment.” The Office Action’s interpretation of this statement ignores the rest of Webb, which, as explained by Dr. Novick, teaches that any further investigations of bcl-2 antisense therapy should be in the direction of longer treatment periods.

The Applicants also note that the Office Action’s statement bridging pages 13 and 14: “Clearly, the disclosed reports of Webb et al. show evidence of reduction in tumor size and tumor response in a human patient and thus constitute a method of treating cancer.” This statement ignores the fact that any reduction in tumor size and

tumor response reported by Webb occurred in patients who where treated for two weeks.

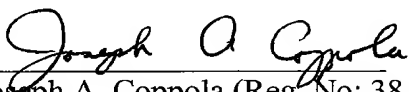
The Applicants further note that the Office Action stated, at page 17: "Webb et al. teach the same method steps as instantly claimed, namely, administering a bcl-2 antisense to a human patient for a cycle of therapy consists [sic] of 3 to 9 days ..." This is incorrect. Webb does not teach that same steps as presently claimed. The present claims require more than one cycle of 3 to 9 days, separated by an interval of at least one day. Webb teaches only a two-week treatment period.

The time for responding to the Office Action was set for November 22, 2007. Enclosed herewith is a Petition for the Extension of Time under 37 C.F.R. § 1.136(a) for a period sufficient to permit the filing of this paper. Charge any fees associated with the Petition for the Extension of Time to Kenyon & Kenyon's Deposit Account No. 11-0600.

The Applicants hereby make a Conditional Petition for any relief available to correct any defect seen in connection with this filing, or any defect seen to be remaining in this application after this filing. The Commissioner is authorized to charge Kenyon & Kenyon's Deposit Account No. 11-0600 for the Petition fee and any other fees required to effect this Conditional Petition.

Respectfully submitted,

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